

## **REMARKS**

Prior to entry of this amendment, claims 1-36 were pending. Claim 1 and 14 are currently amended, and Claim 17 was previously amended in the response filed on 10/09/08. No new matter has been introduced with this amendment. Support for these amendments can be found in the previous claims and page 12-13 of the specification.

For the sake of clarity, the rejections of the presently outstanding Office Action are addressed below in the order in which they were presented.

### **Response to Claim Rejections – 35 USC § 103**

Applicants thank the Examiner for withdrawing the rejections with regards to Brown et al. Claims 1, 35 and 36 were rejected under 35 USC § 103 as being unpatentable over Kovacs et al. (5,981,268) in view of Luo et al. (Bio-Medical Materials and Engineering), or Franks (4,968,623). Examiner argues that “it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the detector array of the primary reference with a thin film of diamond-like carbon material to improve cell adhesion to the surface of the detector array.”

Applicants again disagree that the two cited references, Luo et al. or Franks et al., disclose patterning the thin-film of diamond-like carbon (DLC) material and reiterate the arguments made in the prior responses. While both references teach the use of DLC as a biologically compatible material suitable for use in cell culture, neither Luo et al. or Franks et al., nor any other cited reference, teach that application of DLC could be used to direct or pattern cell growth as Applicants have claimed. This feature is discussed specifically on page 12 of Applicants' specification and shown below.

“The patterning of film 30 is designed to control the connections between neuronal cells in predetermined ways. The material used in patterned film 30 is designed to facilitate neuronal attachment and growth, so that the areas of the device lacking patterned film 30 have essentially no neuronal growth. Accordingly, a neuronal body may be selected for engagement by a dendrite at a pre-determined distance from the center of the neuron by virtue of the arrangement of patterned film 30. The patterned film 30 may also be formed of an electrically conductive metal to be useful for delivering

an electrical signal to a pre-selected neuron.”

Applicants also point to Figure 6, which shows patterned growth of neurons on DLC while there is little to no growth on areas with no DLC. Furthermore, Applicants have also amended independent claim 14 to reflect that cells grown only on the patterned film.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicants respectfully submit that Kovacs et al. does not teach or suggest a cell culture apparatus having a thin patterned film that patterns cell growth, as claimed by Applicants. As such, the Examiner has failed to establish a *prima facie* case of obviousness with regard to claim 1, because the combination of Kovacs et al. in view of Franks et al. or Luo et al. does not teach each and every feature of Applicants' claimed invention. None of the references teaches or suggests the controlled, patterned growth of cells using a patterned film.

Furthermore, there is no teaching, suggestion or motivation to combine these two references with Kovacs et al. to make Applicants' claimed invention. Franks et al. and Luo et al. show examples of using DLC in common cell culture containers such as, vials and microtiter plates as shown in Figure 1 and 2 respectively in Franks et al. In Kovacs et al. the cells are grown either directly on the microelectrode array or in Petri dishes placed on the microelectrodes. None of the photographs, examples or the cellular impedance data gathered in Kovacs et al. utilizes a CCD array, but only show or were obtained by growing cells on the etched microelectrode array or in Petri dishes.

Since according to Kovacs et al. the cells were allowed to adhere to the microelectrodes (col. 15, line 53), there would have been no motivation to use another patterned layer or film to pattern cell growth since it was not known that diamond-like carbon patterned cell growth as described in the present specification. Furthermore, it would have been appreciated by one having skill in the art, that such microelectrode arrays do not react to cell culture media and are not extremely sensitive to exposure to cell culture media as a CCD optical array. Thus,

Applicants assert that it would not have been obvious to use a patterned film of diamond-like carbon to pattern cell growth directly on a CCD array with only thin films to protect the detector array as described in Applicants' claims.

Therefore, Applicants respectfully request that the rejection be withdrawn. In light of the foregoing arguments, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 103 be withdrawn and the claim allowed.

### **Response to Claim Rejections – 35 USC § 103**

The Brown et al. reference was explicitly removed from the previous rejection. Because it would be improper for the Examiner to cite the Brown et al. for rejection of claims 2-33 under 35 U.S.C. § 103(a), Applicants do not include it in the analysis below. Applicants request that the Examiner confirm that the Brown et al. reference has been withdrawn for the present rejection of claims 2-33.

Claims 2-33 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kovacs et al (US 5,981,268) in view of any of Luo et al (Bio-Medical Materials and Engineering) or Franks (US 4,968,623) taken further in view of Miyamoto (US 5,702,915).

Applicants disagree that the combination of the cited references of Kovacs et al, and Luo et al, or Franks et al., and further in view of Miyamoto et al., teach, suggest or motivate the combination of various elements to make Applicants' claimed invention or that it would have been obvious to combine these references to make Applicants' claimed invention. Applicants reiterate that none of the cited references, Kovacs et al., Franks et al. or Luo et al., teach or suggest a cell culture apparatus having a thin patterned film that patterns cell growth on a CCD array, as claimed by Applicants. The addition of a fourth reference, Miyamoto et al. does not cure this defect.

Applicants disagree with the Examiner's reading of Miyamoto as disclosing "that it is known in the cell culture art to interface a cell culture with a CCD array (1)..." Office Action at 4. Indeed, Miyamoto states that "[a]fter charge coupled device (CCD) have been made

available, the element for taking photographs of images of a solid has developed and has been enormously improved...Because of these advantage[s], the element for taking photographs of images of a solid is taking over camera tubes in the field of broadcasting and so on.” Miyamoto clearly is referring to using a CCD to take photographs of a solid and cell activity (col. 1, line 54) and not referring to any known technique of “interfac[ing]” cells with a CCD array.

Neither does Miyamoto teach or suggest interfacing cells with a CCD array as claimed by Applicants. Miyamoto teaches the use of a cell culture container positioned on the upper surface of a solid-state area image pickup element, but does not teach or suggest the use of a thin protective film over the CCD and/or a thin patterned film to pattern cellular growth. Applicants use a thin protective film of micron-range thickness as opposed to the cell culture containers taught by these four cited references which feature centimeter thickness. Heretofore, it has not been shown that thin films could be used and that cells would remain viable for long-term growth (upwards of days and weeks at a time).

Applicants submit that the aspects of the invention of growing cells on a CCD array, using thin film of micron thickness and growing cells in a pattern for long-term growth were unexpected results and demonstrated technology that is a leap forward, not an obvious change from the prior art. Prior to Applicants claimed invention, this invention had not been shown to be possible. Applicants submit that the Examiner has not appreciated this unexpected result of patterning cell growth on a CCD array for long-term growth. Certainly the Examiner can at least appreciate the sensitivity of optical CCD arrays would normally require that the prevention of fluid contact with a CCD array. Growing cells on an optical CCD array for long-term growth is a feat Applicants have demonstrated and so claim. This is well-beyond taking pictures of cells through a cell plate as suggested by Miyamoto. Moreover making films that are both transparent, pattern cell growth and are not permeable to the cell media would not be obvious choices to allow direct interfacing and growth on a CCD array. The present invention represents a leap forward, not just an obvious step away from these references. As evidence of this, Applicants attached a copy of a special press release which describes that Applicants received special

DARPA funding and R&D 100 awards for this technology to the previous response.

Furthermore, the licensee of this technology has received continued DARPA funding for the development of this technology.

Thus, Applicants assert that it was not obvious to combine these references to use a thin protective film directly over the CCD or to use a thin patterned film such as diamond-like carbon to pattern cell growth on a detector array for long-term cell growth and detection. Therefore, Applicants respectfully request that the rejection be withdrawn. In light of the foregoing arguments, Applicants respectfully request that the rejection of claims 2-33 under 35 U.S.C. § 103 be withdrawn and the claims allowed.

### **CONCLUSION**

Accordingly, Applicants respectfully request the entry of the claims as amended and provided herein. A petition for extension of time for the third month of extension and the fee for \$485 is attached. The fee of \$65 for the one month extension paid previously is subtracted from the two months extension fee of \$550. Additionally, the fee of \$405 for the Request for Continued Examination is also enclosed. The Commissioner is hereby authorized to deduct a total of \$890.00 from Deposit Account 120690. Applicants believe all fees necessary for this amendment are submitted herewith. If any additional fee is necessary for entry of this amendment, the Office is hereby authorized to deduct that charge from Deposit Account 120690.

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned at (510)495-2456.

Respectfully submitted,

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By: /Michelle Chew Wong/  
Michelle Chew Wong  
Reg. No. 50,456  
Lawrence Berkeley National Laboratory  
One Cyclotron Road, Mail Stop 56A-120  
Berkeley, California 94720-8127  
Alt. Telephone (510) 486-7058  
Facsimile (510) 486-7896